

General

Guideline Title

Methods for staging non-small cell lung cancer: diagnosis and management of lung cancer, 3rd ed: American College of Chest Physicians evidence-based clinical practice guidelines.

Bibliographic Source(s)

Silvestri GA, Gonzalez AV, Jantz MA, Margolis ML, Gould MK, Tanoue LT, Harris LJ, Detterbeck FC. Methods for staging non-small cell lung cancer: diagnosis and management of lung cancer, 3rd ed: American College of Chest Physicians evidence-based clinical practice guidelines. Chest. 2013 May;143(5 Suppl):e211S-50S. [360 references] [PubMed](#)

Guideline Status

This is the current release of the guideline.

This guideline updates previous versions: Silvestri GA, Gould MK, Margolis ML, Tanoue LT, McCrory D, Toloza E, Detterbeck F, American College of Chest Physicians. Noninvasive staging of non-small cell lung cancer: ACCP evidenced-based clinical practice guidelines (2nd edition). Chest. 2007 Sep;132(3 Suppl):178S-201S.

Detterbeck FC, Jantz MA, Wallace M, Vansteenkiste J, Silvestri GA, American College of Chest Physicians. Invasive mediastinal staging of lung cancer: ACCP evidence-based clinical practice guidelines (2nd edition). Chest. 2007 Sep;132(3 Suppl):202S-20S.

Recommendations

Major Recommendations

The grades of recommendation (1A–2C) and the approach to rating the quality of evidence are defined at the end of the "Major Recommendations" field.

General Approach to Patients

For patients with either a known or suspected lung cancer who are eligible for treatment, a computed tomography (CT) scan of the chest with contrast is recommended (Grade 1B).

Remark: If positron emission tomography (PET) scan is unavailable for staging, the CT of the chest should be extended to include the liver and adrenal glands to assess for metastatic disease.

For patients with either a known or suspected lung cancer, it is recommended that a thorough clinical evaluation be performed to provide an initial definition of tumor stage (Grade 1B).

In patients with either a known or suspected lung cancer who have an abnormal clinical evaluation and no suspicious extrathoracic abnormalities on

chest CT, additional imaging for metastases is recommended (Grade 1B).

Remark: Site specific symptoms warrant directed evaluation of that site with the most appropriate study.

Extrathoracic Staging

In patients with a normal clinical evaluation and no suspicious extrathoracic abnormalities on chest CT being considered for curative-intent treatment, PET imaging (where available) is recommended to evaluate for metastases (except the brain) (Grade 1B).

Remark: Ground glass opacities and an otherwise normal chest CT do not require a PET scan for staging.

Remark: In patients with peripheral stage cIA tumors a PET scan is not required.

Remark: If PET is unavailable, bone scan and abdominal CT are reasonable alternatives to evaluate for extrathoracic disease.

In patients with an imaging finding (e.g., by PET) suggestive of a metastasis, further evaluation of the abnormality with tissue sampling to pathologically confirm the clinical stage is recommended prior to choosing treatment (Grade 1B).

Remark: Tissue sampling of the abnormal site is imperative so that the patient is not excluded from potentially curative treatment.

Remark: Tissue sampling of a distant metastatic site is not necessary if there is overwhelming radiographic evidence of metastatic disease in multiple sites.

Remark: Tissue sampling of the mediastinal lymph nodes does not necessarily need to be performed if there is overwhelming radiographic evidence of metastatic disease in multiple distant sites.

Detection of Brain Metastases

In patients with clinical stage III or IV non-small cell lung cancer (NSCLC) it is suggested that routine imaging of the brain with head magnetic resonance imaging (MRI) (or CT if MRI is not available) should be performed, even if they have a negative clinical evaluation (Grade 2C).

Staging of the Mediastinum

Approach to the Patient

Mediastinal Infiltration

For patients with extensive mediastinal infiltration of tumor and no distant metastases, it is suggested that radiographic (CT) assessment of the mediastinal stage is usually sufficient without invasive confirmation (Grade 2C).

Discrete Mediastinal Node Enlargement

In patients with discrete mediastinal lymph node enlargement (and no distant metastases) with or without PET uptake in mediastinal nodes, invasive staging of the mediastinum is recommended over staging by imaging alone (Grade 1C).

In patients with PET activity in a mediastinal lymph node and normal appearing nodes by CT (and no distant metastases), invasive staging of the mediastinum is recommended over staging by imaging alone (Grade 1C).

In patients with high suspicion of N2,3 involvement, either by discrete mediastinal lymph node enlargement or PET uptake (and no distant metastases), a needle technique (endobronchial ultrasound-needle aspiration [EBUS-NA], endoscopic ultrasound-needle aspiration [EUS-NA] or combined EBUS/EUS-NA) is recommended over surgical staging as a best first test (Grade 1B).

Remark: This recommendation is based on the availability of these technologies (EBUS-NA, EUS-NA, or combined EBUS/EUS-NA) and the appropriate experience and skill of the operator.

Remark: In cases where the clinical suspicion of mediastinal node involvement remains high after a negative result using a needle technique, surgical staging (e.g., mediastinoscopy, video-assisted thoracic surgery [VATS], etc.) should be performed.

Remark: The reliability of mediastinal staging may be more dependent on the thoroughness with which the procedure is performed than by which test is used.

Central and Clinical N1 Nodes

In patients with an intermediate suspicion of N2,3 involvement, i.e., a radiographically normal mediastinum (by CT and PET) and a central tumor

or N1 lymph node enlargement (and no distant metastases), invasive staging of the mediastinum is recommended over staging by imaging alone (Grade 1C).

In patients with an intermediate suspicion of N2,3 involvement, i.e., a radiographically normal mediastinum (by CT and PET) and a central tumor or N1 lymph node enlargement (and no distant metastases), a needle technique (EBUS-NA, EUS-NA, or combined EBUS/EUS-NA) is suggested over surgical staging as a best first test (Grade 2B).

Remark: This recommendation is based on the availability of these technologies (EBUS-NA, EUS-NA, or combined EBUS/EUS-NA) and the appropriate experience and skill of the operator.

Remark: In cases where the clinical suspicion of mediastinal node involvement remains high after a negative result using a needle technique, surgical staging (e.g., mediastinoscopy, VATS, etc.) should be performed.

Remark: The reliability of mediastinal staging may be more dependent on the thoroughness with which the procedure is performed than by which test is used.

Peripheral Stage I Tumors

For patients with a peripheral clinical stage IA tumor (negative nodal involvement by CT and PET), it is suggested that invasive preoperative evaluation of the mediastinal nodes is not required (Grade 2B).

Patients with Left Upper Lobe (LUL) Tumors

For the patients with a LUL cancer in whom invasive mediastinal staging is indicated as defined by the previous recommendations, it is suggested that invasive assessment of the aortopulmonary window (APW) nodes be performed (via Chamberlain, VATS, or extended cervical mediastinoscopy) if other mediastinal node stations are found to be uninvolved (Grade 2B).

Definitions:

Strength of the Recommendations Grading System

| Grade of Recommendation | Benefit vs. Risk and Burdens | Methodologic Quality of Supporting Evidence | Implications |
|--|--|---|--|
| Strong recommendation, high-quality evidence, Grade 1A | Benefits clearly outweigh risk and burdens or vice versa | Consistent evidence from randomized controlled trials (RCTs) without important limitations or exceptionally strong evidence from observational studies | Recommendation can apply to most patients in most circumstances. Further research is very unlikely to change confidence in the estimate of effect |
| Strong recommendation, moderate-quality evidence, Grade 1B | Benefits clearly outweigh risk and burdens or vice versa | Evidence from RCTs with important limitations (inconsistent results, methodologic flaws, indirect or imprecise), or very strong evidence from observational studies | Recommendation can apply to most patients in most circumstances. Higher quality research may well have an important impact on confidence in the estimate of effect and may change the estimate |
| Strong recommendation, low- or very-low-quality evidence, Grade 1C | Benefits clearly outweigh risk and burdens or vice versa | Evidence for at least one critical outcome from observational studies, case series, or from RCTs with serious flaws or indirect evidence | Recommendation can apply to most patients in many circumstances. Higher-quality research is likely to have an important impact on confidence in the estimate of effect and may well change the estimate |
| Weak recommendation, high-quality evidence, Grade 2A | Benefits closely balanced with risks and burden | Consistent evidence from RCTs without important limitations or exceptionally strong evidence from observational studies | The best action may differ depending on circumstances or patient's or societal values. Further research is very unlikely to change confidence in the estimate of effect |
| Weak recommendation, moderate-quality evidence, Grade 2B | Benefits closely balanced with risks and burden | Evidence from RCTs with important limitations (inconsistent results, methodologic flaws, indirect or imprecise) or very strong evidence from observational studies | Best action may differ depending on circumstances or patient's or societal values. Higher-quality research may well have an important impact on confidence in the estimate of effect and may change the estimate |
| Weak | Uncertainty in the | Evidence for at least one critical | Other alternatives may be equally reasonable. |

| Grade of Recommendation | Benefit vs. Risk and Burdens | Methodologic Quality of Supporting Evidence | Implications |
|--|--|--|--|
| recommendation, low or very-low-quality evidence, Grade 2C | estimates of benefits, risks, and burden; benefits, risk, and burden may be closely balanced | outcome from observational studies, case series, or RCTs with serious flaws or indirect evidence | Higher-quality research is likely to have an important impact on confidence in the estimate of effect and may well change the estimate |

Clinical Algorithm(s)

None provided

Scope

Disease/Condition(s)

Non-small cell lung cancer (NSCLC)

Guideline Category

Evaluation

Management

Clinical Specialty

Family Practice

Oncology

Pulmonary Medicine

Radiation Oncology

Thoracic Surgery

Intended Users

Advanced Practice Nurses

Allied Health Personnel

Health Care Providers

Nurses

Patients

Physicians

Psychologists/Non-physician Behavioral Health Clinicians

Social Workers

Guideline Objective(s)

To inform the clinical decisions that must be jointly made by physicians and patients in developing diagnostic, treatment, and management plans so

that they can enhance the benefits and reduce the harms associated with various options

Target Population

Patients with known or suspected lung cancer

Interventions and Practices Considered

1. Computed tomography (CT) with contrast
2. Thorough clinical evaluation
3. Positron emission tomography (PET)
4. Bone scan
5. Tissue sampling
6. Magnetic resonance imaging (MRI)
7. Endobronchial ultrasound-needle aspiration (EBUS-NA)
8. Endoscopic ultrasound (EUS)-NA
9. Combined EBUS/EUS-NA
10. Chamberlain procedure
11. Video-assisted thoracic surgery (VATS)
12. Extended cervical mediastinoscopy

Major Outcomes Considered

- Key outcomes related to positron emission tomography (PET) and positron emission tomography computed tomography (PET-CT) scanning as staging modalities
- Correctly staging lung cancer
- Sensitivity and specificity of PET and CT scanning

Methodology

Methods Used to Collect/Select the Evidence

Hand-searches of Published Literature (Primary Sources)

Searches of Electronic Databases

Description of Methods Used to Collect/Select the Evidence

The authors updated a systematic review of the diagnostic accuracy of different staging methods for patients with non-small cell lung cancer (NSCLC). A more complete description of the methods can be found in the first edition of the American College of Chest Physicians (ACCP) guidelines. Briefly, computerized searches of MEDLINE covering January 1991 to May 2006 for the previous guidelines and January 2006 to June 2012 for this iteration were performed. In addition, the panel searched the reference lists of included studies, practice guidelines, systematic reviews, and meta-analyses to ensure that all relevant studies were identified. Only articles published in English were considered. The search strategy and results are available on request. The searches were structured around the following population, intervention, comparator, outcomes (PICO) questions (detailed in Table 1S in the supporting data [see the "Availability of Companion Documents" field]):

1. What is the role of PET scan in the staging of patients with NSCLC?
2. What is the impact of mediastinal staging by imaging and invasive staging procedures in patients with NSCLC?

Selection Criteria

Titles and abstracts, and the full text of all articles passing the title-and-abstract screen, were evaluated independently by three of the authors for inclusion or exclusion based on the following five criteria: (1) publication in a peer-reviewed journal; (2) a study size of ≥ 20 patients (except for studies involving computed tomography [CT] scan evaluation of the mediastinum or mediastinoscopy, which required a study size of ≥ 50 patients); (3) patient group not included in a subsequent update of the study; (4) for noninvasive staging methods, histologic or cytologic confirmation of mediastinal nodes or extrathoracic sites in addition to the primary tumor; for invasive staging methods, confirmation of mediastinal nodal biopsy results by histology at the time of resection, or long-term clinical follow-up (≥ 1 year); and (5) availability of the raw data needed to calculate independently the sensitivity, specificity, negative predictive value (NPV), and positive predictive value (PPV), or the raw data needed to calculate the NPV of the clinical evaluation. Disagreements were resolved by consensus.

Number of Source Documents

Not stated

Methods Used to Assess the Quality and Strength of the Evidence

Weighting According to a Rating Scheme (Scheme Not Given)

Rating Scheme for the Strength of the Evidence

Not stated

Methods Used to Analyze the Evidence

Review of Published Meta-Analyses

Systematic Review with Evidence Tables

Description of the Methods Used to Analyze the Evidence

The data abstraction was performed for patients suspected of having lung cancer (e.g., non-small cell lung cancer [NSCLC], small cell lung cancer [SCLC]). Where possible, patients suspected of a diagnosis other than lung cancer were excluded. A definite diagnosis of any lung cancer in the mediastinal tissues was considered positive, whereas other diagnoses (benign disease, lymphoma, and so forth) were coded as negative for lung cancer. Equivocal test results were considered negative. Data were abstracted and results were tabulated on a per-patient basis, not per lymph node station. Calculation of subtotal or total summary performance characteristics was accomplished by calculating median of the values (sensitivity, specificity, and other values) from each study; in other words, no weighting according to study size was performed. This method was chosen because of its simplicity. In this iteration of the guidelines, randomized controlled trials (RCTs) comparing the use of noninvasive staging tests with control and those making comparisons among invasive staging techniques are reported separately.

Various parameters, including sensitivity, specificity, PPV, and NPV, can be used to assess the reliability of a test. Sensitivity is defined as the percentage of people with the disease who are detected by the test. (It is calculated as the number of true-positive [TP] results divided by the sum of TP and false-negative [FN] results). Specificity is defined as the percentage of people without the disease who were correctly labeled by the test as not having the disease. (It is calculated as the number of true-negative [TN] results divided by the sum of the TN and false-positive [FP] results.) Sensitivity and specificity are derived from patient populations in whom the true disease status is already known, who either all have or do not have the condition in question. These parameters provide data about how often the test will be positive or negative for these respective populations. Thus, these measures provide information about the test, because the disease status has already been determined in the patients. The PPV is defined as the likelihood that a patient with a positive test result actually has the disease. It is calculated as the number of TP results divided by the sum of the TP and FP results. The NPV is defined as the likelihood that a patient with a negative test result really does not have the disease. It is calculated as the number of TN results divided by the sum of the TN and FN results. Thus, these measures provide information about the disease. Both the PPV and the NPV vary with the prevalence of disease, which is the frequency of disease in the population, and they are calculated as the number of patients with either a TP or an FN result divided by the total number of patients. However, the impact of the prevalence on the NPV and the PPV is minor unless the prevalence is very high or low, respectively; therefore, the NPV (or PPV) from studies with $>80\%$ (or $<20\%$) prevalence are excluded from summary calculations. All these parameters are reported where appropriate.

Assessment of Study Quality

Systematic reviews and meta-analyses were assessed using Documentation and Appraisal Review Tool (DART) (R. L. Diekemper; B. K. Ireland, MD; and L. R. Merz, PhD, MPH, DART, unpublished data, 2012), which was developed as an improved alternative to the existing tools for use in a clinical setting. However, this tool has been adopted for use in American College of Chest Physicians (ACCP) guidelines and consensus statements since 2011.

Quality was assessed for each study as well as for the body of relevant evidence. Based on the population, intervention, comparator, and outcome (PICO) questions and volume of available literature, multiple study designs were included in the systematic reviews of the literature. Randomized controlled trials (RCTs) primarily indicate benefits, but whenever observational studies met inclusion criteria they were often helpful in identifying harms. Observational studies were also examined when RCTs were not available to answer a particular PICO question. Allowing for multiple study designs resulted in the need for multiple quality assessment tools. Tools were chosen for assessing RCTs, observational studies, and diagnostic studies. The quality assessment tool for RCTs (R. L. Diekemper, B. K. Ireland, and L. R. Merz, unpublished data, 2012) was used for assessing the quality of RCTs, and a tool developed by the committee of the ninth edition of the Antithrombotics Guidelines was used for assessing the quality of observational studies. Diagnostic studies were assessed using the Quality Assessment Tool for Diagnostic Accuracy Studies (QUADAS).

Meta-analyses

If a recently published good-quality meta-analysis was available, then it was used to inform the recommendations. When a good-quality meta-analysis was not available, guideline authors were encouraged to perform their own meta-analyses. Meta-analyses were performed when the data were fairly homogeneous. If a study was deemed poor quality, then it was not included in the pooled analysis. Heterogeneity of the pooled results was assessed using a χ^2 test and Higgins I^2 , and a forest plot was examined for consistency of the results. The random effects model was chosen a priori as the appropriate model for pooling the data because it accounts for heterogeneity among the included studies. Results from the meta-analyses are available in the supplementary materials that can be downloaded from the Journal website under the corresponding article in the table of contents.

Methods Used to Formulate the Recommendations

Expert Consensus

Description of Methods Used to Formulate the Recommendations

Panel Composition and Responsibilities

A call for applications to serve on the 3rd edition of the American College of Chest Physicians (ACCP) Lung Cancer Guidelines (LC III) panel was put forth to the ACCP membership, to past panelists, and to other organizations that have previously endorsed earlier editions of these guidelines or appointed representatives to serve on those panels. Guiding the team was the LC III Executive Committee, composed of a Panel Chair, Vice Chair, Liaison to the Guidelines Oversight Committee (GOC), and two staff members, one serving as an adviser and the other as the lead methodologist. The GOC appointed the Liaison and the Chair, who was required to be free of conflicts of interest (COI). This Executive Committee provided general oversight and guidance; multiple reviews of research questions, article outlines, manuscripts, evidence tables, and other supporting documents; and facilitation of the final conference discussions and voting. As the scope was defined, content experts in each major area were identified to serve as topic editors and nominated by the Panel Chair to be advanced to the GOC for the requisite qualifications and COI review and approval process. These topic editors organized their research and writing teams, oversaw the work of the individual members, edited separate contributions into synthesized manuscripts, presented evidence at the final conference, and managed any of their committee members who were approved with management stipulations relevant to their COIs.

Each topic editor was initially charged with proposing individuals to support their topic committees with expertise in the content area and/or methodology. With the Chair's approval, these individuals were nominated for GOC reviews for COI and expertise. In some cases, GOC staff helped to locate additional methodologic support when it was determined to be necessary for various article committees. This resulted in an international panel of >100 multidisciplinary experts across 24 articles representing the fields of pulmonary medicine, critical care medicine, thoracic surgery, medical and radiation oncology, pathology, integrative medicine, primary care, health-care research, guidelines methodology, and epidemiology. Nineteen international organizations that are also dedicated to advancing research and practice in the area of lung cancer were invited to appoint representatives to this guideline project as adjunct participants. These individuals, unless already approved panelists, were not considered full voting members of the panel, since they had not been through the same ACCP COI review, but were included at the final

conference, participated fully in the discussions, and provided external review and feedback on the manuscripts and supporting documentation.

Formulating the Recommendations

In most cases the topic editors, along with the other completely non-conflicted members of the article committee, formulated the recommendations. The summarized evidence tables and profiles (where profiles existed) provided the foundation for the recommendations. In formulating the recommendations, panelists considered not only the body of evidence but also the balance between the benefits and harms and considerations of other factors, such as cost or resource availability considerations and patient values and preferences, which might vary widely for some recommendations. These additional considerations are described in a Remarks section, which appears just below the relevant recommendation in the publication, each time the recommendation appears.

Grading the Recommendations

Recommendations that are strong must be differentiated from those that are weak or weaker. Thus, the ACCP Grading System was used (see the "Rating Scheme for the Strength of the Recommendations" field), and the wording of the recommendations is explicit. This grading system has been used since 2005 and is based on two dimensions: the balance of benefits to harms and the quality of the evidence base. If the benefits clearly outweigh the harms or the harms clearly outweigh the benefits, the strength of the recommendation is considered strong and graded as a 1. In most cases, when there is strong confidence that the benefits outweigh the harms, most patients would choose the intervention endorsed in that recommendation. However, when the tradeoffs between desirable and undesirable consequences are not as clear, variability in patient preferences and values often becomes germane to the decision-making conversation.

Weak recommendations are those for which the benefits and harms are more equally balanced, and thus a clear choice is not as obvious; these are graded with a 2. Strong recommendations are phrased, "the panel recommends," whereas weak recommendations are phrased "the panel suggests." Accompanying these indications of the strength of a recommendation is a letter score (A, B, or C) representing the grading of the body of relevant literature.

In grading the quality of the evidence, RCTs start with a high score but might be downgraded to moderate or even low based on the following criteria: limitations in the study design or conduct of the trial, imprecision, indirectness relative to the specifics of the PICO question, inconsistency in the results, and risk of reporting bias. Observational studies, on the other hand, start off as low-level evidence but can be upgraded to moderate or even high if exceptionally large and consistent treatment effects increase confidence in the findings, especially if there is a strong dose-response gradient.

The final grades are combinations reflecting the strength of the recommendation and the quality of the evidence. Strong recommendations with high quality evidence, grade of 1A, are less common than in past editions of these guidelines, since the evidence is assessed with greater rigor for most topics, and few studies without important limitations are available.

However, recommendations that do attain this score are those for which the panel could state with confidence that new studies would be unlikely to change the direction of the effect. These recommendations apply to most patients in most circumstances. But as the grades decline, patient values and preferences likely would play an increasingly greater role in determining the best treatments or interventions for each patient.

The Final Conference

As the evidence reviews were completed and the tables and profiles prepared, the manuscripts and recommendations were drafted. Members of the article committees convened by phone or e-mail to discuss the evidence and work on drafting and grading the recommendations. These discussions generally resulted in agreement on both the quality of the evidence and strength of the recommendations.

The manuscripts and supporting tables were then reviewed by members of the Executive Committee and, after several iterations, the revised versions were shared among all panelists and the representatives of invited organizations in advance of the conference. The other panelists and representatives were asked not only to provide feedback but also to review the recommendations to identify any controversies. A recommendation was deemed to be controversial if at least one person disagreed with the wording or the grading, if there was controversy in practice, if there were wide variations in practice, or if at least one person asked that it be discussed among the broader panel and association representatives. These identified controversies composed the main agenda for the conference.

See the "Methodology for Development of Guidelines for Lung Cancer" (see the "Availability of Companion Document" field) for more information.

Rating Scheme for the Strength of the Recommendations

| Grade of Recommendation | Benefit vs. Risk and Burdens | Methodologic Quality of Supporting Evidence | Implications |
|--|---|---|--|
| Strong recommendation, high-quality evidence, Grade 1A | Benefits clearly outweigh risk and burdens or vice versa | Consistent evidence from randomized controlled trials (RCTs) without important limitations or exceptionally strong evidence from observational studies | Recommendation can apply to most patients in most circumstances. Further research is very unlikely to change confidence in the estimate of effect |
| Strong recommendation, moderate-quality evidence, Grade 1B | Benefits clearly outweigh risk and burdens or vice versa | Evidence from RCTs with important limitations (inconsistent results, methodologic flaws, indirect or imprecise), or very strong evidence from observational studies | Recommendation can apply to most patients in most circumstances. Higher quality research may well have an important impact on confidence in the estimate of effect and may change the estimate |
| Strong recommendation, low- or very-low-quality evidence, Grade 1C | Benefits clearly outweigh risk and burdens or vice versa | Evidence for at least one critical outcome from observational studies, case series, or from RCTs with serious flaws or indirect evidence | Recommendation can apply to most patients in many circumstances. Higher-quality research is likely to have an important impact on confidence in the estimate of effect and may well change the estimate |
| Weak recommendation, high-quality evidence, Grade 2A | Benefits closely balanced with risks and burden | Consistent evidence from RCTs without important limitations or exceptionally strong evidence from observational studies | The best action may differ depending on circumstances or patient's or societal values. Further research is very unlikely to change confidence in the estimate of effect |
| Weak recommendation, moderate-quality evidence, Grade 2B | Benefits closely balanced with risks and burden | Evidence from RCTs with important limitations (inconsistent results, methodologic flaws, indirect or imprecise) or very strong evidence from observational studies | Best action may differ depending on circumstances or patient's or societal values. Higher-quality research may well have an important impact on confidence in the estimate of effect and may change the estimate |
| Weak recommendation, low- or very-low-quality evidence, Grade 2C | Uncertainty in the estimates of benefits, risks, and burden; benefits, risk, and burden may be closely balanced | Evidence for at least one critical outcome from observational studies, case series, or RCTs, with serious flaws or indirect evidence | Other alternatives may be equally reasonable. Higher-quality research is likely to have an important impact on confidence in the estimate of effect and may well change the estimate |

Cost Analysis

- Since the publication of the last American College of Chest Physicians (ACCP) lung cancer guidelines, several studies have evaluated additional key outcomes related to positron emission tomography (PET) and PET-computed tomography (CT) scanning as staging modalities and have compared them with conventional staging (bone scan, abdominal CT scan). In general, these analyses suggest that PET scanning is cost effective compared with CT scanning and correlates better with long-term outcomes.
- The cost of endoscopic ultrasound (EUS) is lower than that of surgical staging procedures, probably because of the ability to perform EUS without general anesthesia in an ambulatory setting. Two studies have suggested that EUS may be more cost effective than mediastinoscopy, although these studies assumed that mediastinoscopy frequently required inpatient admission.
- There is evidence that the use of PET scanning decreases the number of noncurative resections and may be cost effective in patients with non-small cell lung cancer (NSCLC).

Method of Guideline Validation

External Peer Review

Internal Peer Review

Description of Method of Guideline Validation

Internal and External Peer Review

Once Executive Committee approval was received, the articles were submitted to American College of Chest Physicians (ACCP) staff for several layers of review. All reviewers were required to undergo a full conflict of interest (COI) appraisal before being approved. In the first round of reviews, the Thoracic Oncology NetWork reviewed the content of the manuscripts and the members of the Guidelines Oversight Committee (GOC) assessed the manuscripts for adherence to the methodology and conformance with the evidence. The ACCP President also appointed members of the Board of Regents to evaluate the guidelines in depth. All comments were collated into spreadsheets to ensure that they were appropriately answered. GOC and board reviewers discussed each comment and determined which should be mandatory for the authors to amend and which were provided as suggestions for improvement. All reviews and comments were anonymous, and authors were required to respond to all mandatory issues either by revising the manuscripts or providing written justification explaining why they did not agree with the reviewers' comments.

The revised manuscripts were submitted for round II review, simultaneously with the Journal peer review. Once the GOC and board reviewers approved the manuscripts, the ACCP President, President Elect, President Elect Designee, and Immediate Past President reviewed the guidelines. Approval was granted pending confirmation from the Board of Regents, before submission to the journal for final review by the Journal Editor. In addition to this extensive review process, which included nearly 30 individual reviewers from the ACCP leadership, external organizations were provided with opportunities to provide feedback before, during, and just after the conference. This final version was submitted for consideration for endorsement to all of the invited organizations, whether or not they sent representatives to the conference. However, once the guidelines were approved by the ACCP Board of Regents, no further changes were accepted. Organizations that provided endorsements are listed in each article.

Evidence Supporting the Recommendations

Type of Evidence Supporting the Recommendations

The type of supporting evidence is identified and graded for each recommendation (see the "Major Recommendations" field).

Benefits/Harms of Implementing the Guideline Recommendations

Potential Benefits

Appropriate staging of non-small cell lung cancer

Potential Harms

- A potential harm of positron emission tomography (PET) scanning is that if suspected PET scan findings are not confirmed, patients may be erroneously directed away from a potentially curative resection. Although PET scanning clearly has the potential to be of benefit, in a less structured setting it also has the potential to be of harm if confirmation of the findings is not pursued.
- False-positive (FP) and false-negative (FN) results of imaging
- Complications of invasive staging procedures

Qualifying Statements

Qualifying Statements

- American College of Chest Physicians (ACCP) guidelines are intended for general information only, are not medical advice, and do not replace professional medical care and physician advice, which always should be sought for any medical condition. The complete disclaimer for this guideline can be accessed at the [CHEST Web site](#) .

- Although the ACCP is moving toward the production of evidence profiles for all guideline recommendations, there were many recommendations for which profiles were not developed, mostly because of resource constraints. When possible, methodologists created evidence profiles, and all panelists were educated on how to read and interpret them. The population, intervention, comparator, and outcome (PICO)-based systematic literature review process was followed for most recommendations, but there were some that could have benefited from meta-analyses.
- One limitation of all guidelines today is that they are not able to adequately address complex patients with multiple morbidities. This is largely because these patients are generally excluded from clinical trials and are often not included in observational studies. Since guidelines are reliant on evidence published in the peer-reviewed literature, the scientific foundation impedes the process of providing good guidance for these patients and is a limitation in these guidelines. Therefore, the ACCP encourages funding agencies to ensure that topics with limited evidence are addressed in future research.

Implementation of the Guideline

Description of Implementation Strategy

Dissemination and Implementation

These guidelines are widely disseminated through the *CHEST* journal publication, National Guideline Clearinghouse, and Guidelines International Network library. Additional clinical resources will soon be available to users of CHEST Evidence, an upcoming tool for searching the content of American College of Chest Physicians (ACCP) guidelines.

As the expanding research into diagnostic techniques and treatment options continues to evolve, the guidelines must be updated and kept current. This edition of the ACCP Lung Cancer Guidelines will be the last to be published as a complete collection, as the ACCP is now embarking on a new living guidelines model (LGM) for revising existing recommendations and developing new recommendations as the literature evolves. This will include a continual assessment of the currency of these recommendations relevant to new research studies as they are published. The review cycle for the ACCP Lung Cancer Guidelines will begin 1 year after publication unless the content experts who monitor the literature bring a recommendation or set of related recommendations to the attention of the Guideline oversight Committee (GOC), suggesting that those recommendations are in need of updating sooner. The new LGM will permit a more nimble approach to guideline development but also requires a point-of-care accessible vehicle, CHEST Evidence, for the users to readily search for the most current version. These features will be described in greater detail in upcoming publications. As a step in this direction, these guidelines will be published primarily online with a printed version of the Executive Summary, containing all of the recommendations, the introduction, and this article on methodology. All narratives for each article with their supporting tables, figures, and algorithms will be available online at journal.publications.chestnet.org .

Implementation Tools

Mobile Device Resources

Patient Resources

Quick Reference Guides/Physician Guides

Resources

For information about availability, see the *Availability of Companion Documents* and *Patient Resources* fields below.

Institute of Medicine (IOM) National Healthcare Quality Report Categories

IOM Care Need

Living with Illness

IOM Domain

Effectiveness

Patient-centeredness

Identifying Information and Availability

Bibliographic Source(s)

Silvestri GA, Gonzalez AV, Jantz MA, Margolis ML, Gould MK, Tanoue LT, Harris LJ, Detterbeck FC. Methods for staging non-small cell lung cancer: diagnosis and management of lung cancer, 3rd ed: American College of Chest Physicians evidence-based clinical practice guidelines. Chest. 2013 May;143(5 Suppl):e211S-50S. [360 references] [PubMed](#)

Adaptation

Not applicable: The guideline was not adapted from another source.

Date Released

2003 Jan (revised 2013 May)

Guideline Developer(s)

American College of Chest Physicians - Medical Specialty Society

Source(s) of Funding

- The development of this guideline was supported primarily by the American College of Chest Physicians (ACCP). The lung cancer guidelines conference was supported in part by a grant from the Lung Cancer Research Foundation. The publication and dissemination of the guidelines was supported in part by a 2009 independent educational grant from Boehringer Ingelheim Pharmaceuticals, Inc.
- Role of sponsors: The ACCP was solely responsible for the development of these guidelines. The remaining supporters played no role in the development process. External supporting organizations cannot recommend panelists or topics, nor are they allowed prepublication access to the manuscripts and recommendations. Further details on the Conflict of Interest (COI) Policy are available online at <http://chestnet.org> .
- See the methodology companion (see the "Availability of Companion Documents" field) for a complete discussion of the source of funding for this guideline.

Guideline Committee

American College of Chest Physicians (ACCP) Expert Panel on Lung Cancer Guidelines

Composition of Group That Authored the Guideline

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Financial Disclosures/Conflicts of Interest

- Conflicts of Interest (COI) grids reflecting the conflicts of interest that were current as of the date of the conference and voting are posted in the online supplementary materials.
- Financial/nonfinancial disclosures: The authors have reported to *CHEST* that no potential conflicts of interest exist with any companies/organizations whose products or services may be discussed in this article.
- See the methodology companion (see the "Availability of Companion Documents" field) for a complete discussion of the conflict of interest procedures and requirements for the guideline panel.

Guideline Endorser(s)

American Association for Bronchology and Interventional Pulmonology - Medical Specialty Society

European Society of Thoracic Surgeons - Professional Association

Oncology Nursing Society - Professional Association

Society of Thoracic Surgeons - Medical Specialty Society

Guideline Status

This is the current release of the guideline.

This guideline updates previous versions: Silvestri GA, Gould MK, Margolis ML, Tanoue LT, McCrory D, Toloza E, Detterbeck F, American College of Chest Physicians. Noninvasive staging of non-small cell lung cancer: ACCP evidenced-based clinical practice guidelines (2nd edition). *Chest*. 2007 Sep;132(3 Suppl):178S-201S.

Detterbeck FC, Jantz MA, Wallace M, Vansteenkiste J, Silvestri GA, American College of Chest Physicians. Invasive mediastinal staging of lung cancer: ACCP evidence-based clinical practice guidelines (2nd edition). *Chest*. 2007 Sep;132(3 Suppl):202S-20S.

Guideline Availability

Electronic copies: Available to subscribers of [Chest - The Cardiopulmonary and Critical Care Journal](#) . Also available to Chest subscribers through the [Chest app](#) for iPhone and iPad.

Print copies: Available from the American College of Chest Physicians, Products and Registration Division, 3300 Dundee Road, Northbrook IL 60062-2348.

Availability of Companion Documents

The following are available:

- Methods for staging non-small cell lung cancer: diagnosis and management of lung cancer, 3rd ed: American College of Chest Physicians evidence-based clinical practice guidelines. Supporting data. Electronic copies: Available to subscribers of [Chest - The Cardiopulmonary and Critical Care Journal](#) .
- Detterbeck FC, Zelman Lewis S, Diekemper R, Addrizzo-Harris D, Alberts MW. Diagnosis and management of lung cancer, 3rd ed: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines. Executive summary. *Chest* 2013 May;143(5 Suppl):7S-37S. Electronic copies: Available from the [Chest - The Cardiopulmonary and Critical Care Journal Web site](#) .
- Alberts WM. Introduction to the third edition: diagnosis and management of lung cancer, 3rd ed: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines. *Chest* 2013 May;143(5 Suppl):38S-40S. Electronic copies: Available from the [Chest - The Cardiopulmonary and Critical Care Journal Web site](#) .
- Zelman Lewis S, Diekemper R, Addrizzo-Harris DJ. Methodology for development of guidelines for lung cancer: diagnosis and management of lung cancer, 3rd ed: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines. *Chest* 2013 May;143(5 Suppl):41S-e50S. Electronic copies: Available from the [Chest - The Cardiopulmonary and Critical Care Journal Web site](#) .

- Alberg AJ, Brock MV, Ford JG, Samet JM, Spivack SD. Epidemiology of lung cancer: diagnosis and management of lung cancer, 3rd ed: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines. Chest 2013 May;143(5 Suppl):e1S-e29S. Electronic copies: Available to subscribers of [Chest - The Cardiopulmonary and Critical Care Journal](#) .
- Nana-Sinkham SP, Powell CA. Molecular biology of lung cancer: diagnosis and management of lung cancer, 3rd ed: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines. Chest 2013 May;143(5 Suppl):e30S-e39S. Electronic copies: Available to subscribers of [Chest - The Cardiopulmonary and Critical Care Journal](#) .
- Dettmerbeck FC, Postmus PE, Tanoue LT. The stage classification of lung cancer: diagnosis and management of lung cancer, 3rd ed: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines. Chest 2013 May;143(5 Suppl):e191S-e210S. Electronic copies: Available to subscribers of [Chest - The Cardiopulmonary and Critical Care Journal](#) .

Print copies: Available from the American College of Chest Physicians, Products and Registration Division, 3300 Dundee Road, Northbrook IL 60062-2348.

The following is also available:

- Highlights of the ACCP diagnosis and management of lung cancer guidelines, 3rd ed. Podcast. Available from the [Chest - The Cardiopulmonary and Critical Care Journal Web site](#) .

A lung cancer staging calculator is available from the [Staging Lung Cancer Web site](#) .

Patient Resources

The following are available:

- Lung cancer: understanding the diagnosis. Northbrook (IL): American College of Chest Physicians; 2010. 7 p. Electronic copies: Available in Portable Document Format (PDF) from the [OneBreath.org Web site](#) .
- Understanding non-small cell lung cancer. A guide for the patient. Northbrook (IL): American College of Chest Physicians; 2010. 13 p. Electronic copies: Available in PDF from the [OneBreath.org Web site](#) .

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NGC Status

This NGC summary was completed by ECRI on July 22, 2003. The information was verified by the guideline developer on August 18, 2003. This NGC summary was updated by ECRI Institute on November 9, 2007. The updated information was verified by the guideline developer on December 21, 2007. This NGC summary was updated by ECRI Institute on August 21, 2013.

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